PB86-134210

Health Effects Assessment for Chloroform

(U.S.) Environmental Protection Agency
Cincinnati, OH

Sep 84

U.S. Department of Commerce
National Technical Information Service
NTIS

PB86-134210

EPA/540/1-86/010
September 1984

HEALTH EFFECTS ASSESSMENT FOR CHLOROFORM

U.S. Environmental Protection Agency
Office of Research and Development
Office of Health and Environmental Assessment
Environmental Criteria and Assessment Office
Cincinnati, OH 45268

U.S. Environmental Protection Agency
Office of Emergency and Remedial Response
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Washington, DC 20460

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NATIONAL TECHNICAL
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U.S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA. 22161

TECHNICAL REPORT DATA
(Please read Instructions on the reverse before completing)

1. REPORT NO.	2.	3. RECIPIENT'S ACCESSION NO.
EPA/540/1-86/010		PB86 134210/AS

4. TITLE AND SUBTITLE	5. REPORT DATE
Health Effects Assessment for Chloroform	September 1984
	6. PERFORMING ORGANIZATION CODE: EPA/600/22
7. AUTHOR(S)	8. PERFORMING ORGANIZATION REPORT NO.
9. PERFORMING ORGANIZATION NAME AND ADDRESS Environmental Criteria and Assessment Office Office of Research and Development U.S. Environmental Protection Agency Cincinnati, OH 45268	10. PROGRAM ELEMENT NO. 11. CONTRACT/GRANT NO.
12. SPONSORING AGENCY NAME AND ADDRESS Office of Emergency and Remedial Response Office of Solid Waste and Emergency Response U.S. Environmental Protection Agency Washington, DC 20460	13. TYPE OF REPORT AND PERIOD COVERED 14. SPONSORING AGENCY CODE

15. SUPPLEMENTARY NOTES

16. ABSTRACT

This document represents a brief, quantitatively oriented scientific summary of health effects data. It was developed by the Environmental Criteria and Assessment Office to assist the Office of Emergency and Remedial Response in establishing chemical-specific health-related goals of remedial actions. If applicable, chemical-specific subchronic and chronic toxicity interim acceptable intakes are determined for systemic toxicants, or q_1^* values are determined for carcinogens for both oral and inhalation routes.

A q_1^* was determined for chloroform based on oral exposure.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group

18. DISTRIBUTION STATEMENT	19. SECURITY CLASS (This Report)	21. NO. OF PAGES
Public	Unclassified	32
	20. SECURITY CLASS (This page)	22. PRICE
	Unclassified	

EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE

DISCLAIMER

This report has been funded wholly or in part by the United States Environmental Protection Agency under Contract No. 68-03-3112 to Syracuse Research Corporation. It has been subject to the Agency's peer and administrative review, and it has been approved for publication as an EPA document. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

PREFACE

This report summarizes and evaluates information relevant to a preliminary interim assessment of adverse health effects associated with chloroform. All estimates of acceptable intakes and carcinogenic potency presented in this document should be considered as preliminary and reflect limited resources allocated to this project. Pertinent toxicologic and environmental data were located through on-line literature searches of the Chemical Abstracts, TOXLINE, CANCERLINE and the CHEMFATE/DATALOG data bases. The basic literature searched supporting this document is current up to September, 1984. Secondary sources of information have also been relied upon in the preparation of this report and represent large-scale health assessment efforts that entail extensive peer and Agency review. The following Office of Health and Environmental Assessment (OHEA) sources have been extensively utilized:

U.S. EPA. 1980b. Ambient Water Quality Criteria for Chloroform. Environmental Criteria and Assessment Office, Cincinnati, OH. EPA 440/5-80-033. NTIS PB 81-117442. (Cited in U.S. EPA, 1982)

U.S. EPA. 1982. Hazard Profile for Chloroform. Prepared by the Environmental Criteria and Assessment Office, Cincinnati, OH, OHEA for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1983b. Review of Toxicological Data in Support of Evaluation for Carcinogenic Potential of Chloroform. Prepared by the Carcinogen Assessment Group, OHEA, Washington, DC for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1984. Health Assessment Document for Chloroform. Environmental Criteria and Assessment Office, Research Triangle Park, NC. EPA 600/8-84-004A. NTIS PB 84-195163.

The intent in these assessments is to suggest acceptable exposure levels whenever sufficient data were available. Values were not derived or larger uncertainty factors were employed when the variable data were limited in scope tending to generate conservative (i.e., protective) estimates. Nevertheless, the interim values presented reflect the relative degree of hazard associated with exposure or risk to the chemical(s) addressed.

Whenever possible, two categories of values have been estimated for systemic toxicants (toxicants for which cancer is not the endpoint of concern). The first, the AIS or acceptable intake subchronic, is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs during a limited time interval (i.e., for an interval that does not constitute a significant portion of the lifespan). This type of exposure estimate has not been extensively used or rigorously defined, as previous risk assessment efforts have been primarily directed towards exposures from toxicants in ambient air or water where lifetime exposure is assumed. Animal data used for AIS estimates generally include exposures with durations of 30-90 days. Subchronic human data are rarely available. Reported exposures are usually from chronic occupational exposure situations or from reports of acute accidental exposure.

The AIC, acceptable intake chronic, is similar in concept to the ADI (acceptable daily intake). It is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs for a significant portion of the lifespan [see U.S. EPA (1980a) for a discussion of this concept]. The AIC is route specific and estimates acceptable exposure for a given route with the implicit assumption that exposure by other routes is insignificant.

Composite scores (CSs) for noncarcinogens have also been calculated where data permitted. These values are used for ranking reportable quantities; the methodology for their development is explained in U.S. EPA (1983a).

For compounds for which there is sufficient evidence of carcinogenicity, AIS and AIC values are not derived. For a discussion of risk assessment methodology for carcinogens refer to U.S. EPA (1980a). Since cancer is a process that is not characterized by a threshold, <u>any</u> exposure contributes an increment of risk. Consequently, derivation of AIS and AIC values would be inappropriate. For carcinogens, q_1^*s have been computed based on oral and inhalation data if available.

ABSTRACT

In order to place the risk assessment evaluation in proper context, the reader is referred to the preface of this document. The preface outlines limitations applicable to all documents of this series as well as the appropriate interpretation and use of the quantitative estimates.

Chloroform has been shown to be carcinogenic by the oral route in rodents in several independent investigations. Human data are limited, but suggestive. The Carcinogen Assessment Group (U.S. EPA, 1984) has used the following data: liver tumors in female mice (NCI, 1976); liver tumors in male mice (NCI, 1976); kidney tumors in male rats (NCI, 1976); and kidney tumors in male mice (Roe et al., 1979). There was no compelling reason to select any one of these data sets over the others; therefore, the geometric mean of the slope (q_1^*), 7×10^{-2} $(mg/kg/day)^{-1}$, was used.

Data are not available which would allow an assessment of the carcinogenic potential of chloroform following inhalation exposure.

ACKNOWLEDGEMENTS

The initial draft of this report was prepared by Syracuse Research Corporation under Contract No. 68-03-3112 for EPA's Environmental Criteria and Assessment Office, Cincinnati, OH. Dr. Christopher DeRosa and Karen Blackburn were the Technical Project Monitors and Helen Ball was the Project Officer. The final documents in this series were prepared for the Office of Emergency and Remedial Response, Washington, DC.

Scientists from the following U.S. EPA offices provided review comments for this document series:

Environmental Criteria and Assessment Office, Cincinnati, OH
Carcinogen Assessment Group
Office of Air Quality Planning and Standards
Office of Solid Waste
Office of Toxic Substances
Office of Drinking Water

Editorial review for the document series was provided by:

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LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
AIC	Acceptable intake chronic
AIS	Acceptable intake subchronic
bw	Body weight
CAS	Chemical abstract service
CS	Composite score
LOAEL	Lowest-observed-adverse-effect level
ppm	Parts per million
STEL	Short-term exposure limit
TLV	Threshold limit value
TWA	Time-weighted average

1. ENVIRONMENTAL CHEMISTRY AND FATE

The relevant physical and chemical properties and environmental fate of chloroform (CAS No. 67-66-3) are as follows:

Chemical class:	halogenated aliphatic hydrocarbon (purgeable halocarbon)
Molecular weight:	119.38 (Callahan et al., 1979)
Vapor pressure:	150.5 mm Hg at 20°C (Callahan et al., 1979)
Water solubility:	8200 mg/ℓ at 20°C (Callahan et al., 1979)
Octanol/water partition coefficient:	93 (Callahan et al., 1979)
Soil mobility: (predicted as retardation factor for a soil depth of 140 cm and organic carbon content of 0.087%)	1.2 (Wilson et al., 1981)
Bioconcentration factor: (in bluegill, Lepomis macrochirus)	6 (Barrows et al., 1978)
Half-life in air:	80 days (U.S. EPA, 1982)
Half-life in water:	0.3-3 days in rivers (Zoeteman et al., 1980) 3-30 days in lakes (Zoeteman et al., 1980)

The half-life of chloroform in soil could not be located in the literature searched. However, evaporation is expected to be the predominant loss mechanism from the soil surface. The half-life for soil evaporation should be longer than its evaporation half-life from water. In subsurface soil, biodegradation of chloroform is likely to be a weak, very slow process (no degradation in 27 weeks) (Wilson et al., 1983). Therefore, in subsurface soil, chloroform is expected to remain stable enough to leach into groundwater.

2. ABSORPTION FACTORS IN HUMANS AND EXPERIMENTAL ANIMALS

2.1. ORAL

Evidence from human assays (Fry et al., 1972), as well as from animal experiments (Brown et al., 1974; Taylor et al., 1974), indicates that ~100% of ingested chloroform is absorbed from the gastrointestinal tract.

2.2. INHALATION

From 49-77% of the chloroform present in the inspired air is absorbed by the lungs (U.S. EPA, 1980b).

3. TOXICITY IN HUMANS AND EXPERIMENTAL ANIMALS

3.1. SUBCHRONIC

Table 3-1 presents a summary of the effects of subchronic chloroform exposure.

3.1.1. Oral. DeSalva et al. (1975) reported that chloroform at dose levels of 1.0 and 2.5 mg/kg/day for a 1-year period produced no effects on the functioning of the human liver and kidney.

No effects in rats were reported at dose levels of 15 and 30 mg/kg/day (Palmer et al., 1979). However, dose levels of 150 and 410 mg/kg/day produced severe toxic effects, such as necrosis of the liver and dysfunction of the gonads (Palmer et al., 1979).

3.1.2. Inhalation. Torkelson et al. (1976) exposed rats, guinea pigs and rabbits to 25, 50 and 80 ppm (122, 244 and 415 mg/m^3, respectively) for 7 hours/day, 4 days/week for 6 months (Table 3-1). Exposure to 25 ppm chloroform produced histopathological changes in the livers and kidneys of male but not female rats. At higher doses, lobular granular degeneration and focal necrosis were increased in the liver, and cloudy swelling of epithelial cells was increased in the kidney. These changes were reported to be reversible after 6 weeks. Hematological, clinical chemistry and urinalysis values were "within normal limits." The results obtained from chloroform exposure in guinea pigs and rabbits are difficult to interpret because adverse effects are seen at the low dose (25 ppm) and high dose (85 ppm) levels, but no effects are reported at the intermediate dose level (50 ppm).

Epidemiological studies of humans exposed to chloroform in the workplace at levels ranging from 22-237 ppm have indicated that depression, gastrointestinal disturbances (e.g., flatulence, nausea), headache and frequent and scalding urination are the primary symptoms (Challen et al., 1958;

TABLE 3-1

Subchronic Toxicity of Chloroform

Route	Dose or Exposure	Duration of Treatment	Species/Strain	Sex	Number Treated	Effect	Reference
Inhalation	0 ppm 25 ppm (122 mg/m³) 50 ppm (244 mg/m³) 85 ppm (415 mg/m³) 25 ppm (122 mg/m³)	7 hours/day, 5 days/week for 6 months 4 hours/day, 5 days/week	rats/NR	M/F M/F M/F M/F M/F	10-12 10-12 10-12 10-12 10	Exposure to chloroform at 25 ppm for 4 hours/day had no effect on male mice; at 25 ppm for 7 hours/day, histopathologic changes in the liver were present in males but not females; at higher doses, increasingly pronounced changes were present in the liver and kidneys of both sexes.	Torkelson et al., 1976
Inhalation	0 ppm 25 ppm (122 mg/m³) 50 ppm (244 mg/m³) 85 ppm (415 mg/m³)	7 hours/day, 5 days/week up to 203 days	guinea pigs/NR	M/F M/F M/F M/F	16-24 16-24 16-24 16-24	Pneumonitis was seen in females exposed to 85 ppm, and histopathological changes were observed in the livers and kidneys of both sexes exposed to 25 ppm but not 50 ppm.	Torkelson et al., 1976
Inhalation	0 ppm 25 ppm (122 mg/m³) 50 ppm (244 mg/m³) 85 ppm (415 mg/m³)	7 hours/day, 5 days/week up to 203 days	rabbits/NR	M/F M/F M/F M/F	4-6 4-6 4-6 4-6	Hepatic and renal pathology was seen in females exposed to 85 ppm, and pneumonitis and hepatic necrosis in males exposed to 85 ppm. Histopathological changes were observed in the livers and kidneys of both sexes exposed to 25 ppm but not 50 ppm.	Torkelson et al., 1976
Oral	0 1.0 mg/kg/day 2.5 mg/kg/day	1 year	human	NR	NR	Liver and kidney function tests indicated that there were no statistically significant differences between chloroform-treated individuals and controls.	DeSalva et al., 1975
Oral	0 15 mg/kg/day 30 mg/kg/day 150 mg/kg/day 410 mg/kg/day	13 weeks	rats/ Sprague-Dawley	M/F	20 20 20 20 20	Increased liver weight with fatty necrosis, gonadal atrophy and cellular proliferation in the bone marrow occurred at 410 and 150 mg/kg/day. No effects were reported for dose levels of 30 and 15 mg/kg/day.	Palmer et al., 1979

NR = Not reported

Bomski et al. 1967). Regarding long-term effects, Challen et al. (1958) reported that there was no evidence of any organic lesion attributable to chloroform, based on physical exams and liver function tests. Bomski et al. (1967) reported that chloroform exposure may result in an increased incidence of viral hepatitis, splenomegaly and hepatomegaly, although no statistical analysis was presented.

3.2. CHRONIC

3.2.1. Oral. Several chronic oral studies (NCI, 1976; Palmer et al., 1979; Roe et al., 1979) were designed to test the carcinogenicity of chloroform (see Chapter 4). However, depression of body weight was observed at chloroform doses $\geq$60 mg/kg/day in rats (NCI, 1976; Palmer et al., 1979) and mice (Roe et al., 1979). Decreased relative liver weight and serum cholinesterase levels were reported in female mice treated with 60 mg/kg/day chloroform (Palmer et al., 1979.) Higher chloroform doses (90 and 180 mg/kg/day) resulted in an increased incidence of noncancerous respiratory diseases in rats (NCI, 1976), and a dose of 477 mg/kg/day resulted in decreased female survival time in mice (NCI, 1976). A dose level of 165 mg/kg/day caused liver necrosis and gonadal atrophy in rats (Palmer et al., 1979). No effects were reported to occur in rats at a dose of 15 mg/kg/day (Palmer et al., 1979).

Chronic exposure of humans to chloroform appears to result in adverse effects on the central nervous system (NIOSH, 1974), although there are no data on the dose relation of the effects. In addition, chloroform affects the liver, kidneys and heart in humans (NIOSH, 1974). The potential for chronic human oral exposure to chloroform has increased because of the widespread practice of chlorinating drinking water (U.S. EPA, 1980b).

3.2.2. Inhalation. Pertinent data regarding the carcinogenicity of chloroform inhalation in humans were not located in the available literature.

3.3. TERATOGENICITY AND OTHER REPRODUCTIVE EFFECTS

Teratogenic effects (acaudia, imperforate anus, decreased crown-rump length, missing ribs and delayed skeletal ossification) were seen in Sprague-Dawley rats (Schwetz et al., 1974) that inhaled chloroform for 7 hours/day on days 6-15 of gestation at dose levels of 30, 100 and 300 ppm (147, 489 and 1466 mg/m^3, respectively). When CF/1 mice (Murray et al., 1979) were exposed to 100 ppm chloroform for 7 hours/day on days 6-15 of gestation, there was a significantly increased incidence of cleft palate. When pregnant mice and rats were exposed to 100 ppm chloroform, their food consumption and body weight decreased, but their relative liver weight increased (U.S. EPA, 1982). Ingestion of chloroform caused fetotoxicity but not teratogenicity, and only at levels that also produced severe maternal toxicity (Thompson et al., 1974).

3.4. TOXICANT INTERACTIONS

The substances that potentiate the toxic effects of chloroform are methyl n-butyl ketone (Branchflower and Pohl, 1981), alcohol (Kutob and Plaa, 1961), carbon tetrachloride (Harris et al., 1982), chlordecone (Iijima et al., 1983), DDT and phenobarbital (McLean, 1970). Methyl n-butyl ketone increases the toxicity of chloroform by lowering glutathione levels and by increasing the levels of hepatic cytochrome P-450, which, in turn, increases the metabolism of chloroform to phosgene (Branchflower and Pohl, 1981). Harris et al. (1982) reported that carbon tetrachloride potentiated the toxic effects of chloroform, because of increased phosgene formation and the initiation of lipid peroxidation. The mechanism of interaction for alcohol, chlordecone, DDT and phenobarbital was not discussed. von Oettingen (1964) reported that high-fat/low-protein diets potentiated the hepatotoxic effects of chloroform in animals.

4. CARCINOGENICITY

4.1. HUMAN DATA

4.1.1. Oral. Although chloroform has not unequivocally been shown to cause human cancer, ecological and case control studies (Alavanja et al., 1978; Cantor et al., 1978; Brenniman et al., 1978; Hogan et al., 1979; Struba, 1979; Gottlieb et al., 1981; Young et al., 1981) have consistently supported the association of increased risk of bladder, colon and rectal cancer with exposure to chloroform, which is the predominant trihalomethane contaminating chlorinated drinking water (U.S. EPA, 1983b).

4.1.2. Inhalation. Although exposure to airborne chloroform in the workplace may have caused toxic effects (Challen et al., 1958; Bomski et al., 1967), and although inhalation of chloroform was teratogenic in rats (Schwetz et al., 1974), pertinent data regarding an association between chloroform inhalation and an increased incidence or risk of cancer were not located in the available literature.

4.2. BIOASSAYS

4.2.1. Oral. Table 4-1 summarizes the available data from oral bioassays of chloroform carcinogenicity. Eschenbrenner and Miller (1945) emphasized that a dose level of chloroform that caused hepatic necrosis when given once would cause hepatic carcinoma when given repeatedly. The NCI (1976) found a dose-related increase in hepatomas in both sexes when mice received chloroform in corn oil by gavage, and an increase in renal epithelial tumors in males when rats received chloroform in corn oil by gavage (Table 4-1). The increased incidence of hepatic and renal tumors was statistically significant ($p<0.05$). Palmer et al. (1979) criticized the NCI study because rats being treated with other volatile carcinogenic substances were housed in the same room as the chloroform-treated rats.

TABLE 4-1

Oral Bioassays of Chloroform Carcinogenicity

Vehicle	Dose	Duration of Treatment	Duration of Study	Species/Strain	Sex	Number Treated	Target Organ	Effects	Reference
NR	150 mg/kg bw 200 mg/kg bw 600 mg/kg bw 1200 mg/kg bw 2400 mg/kg bw	once every 4 days for a total of 30 doses	NR	mice/ (strain A)	NR	NR	liver	Doses of 150 and 300 mg/kg bw produced neither necrosis nor carcinoma in the liver. Doses of 600-2400 mg/kg bw produced necrosis when given once, and hepatomas when given repeatedly. All females at the highest dose and all males at the three highest doses died early in the experiment.	Eschenbrenner and Miller, 1945
Corn oil	0 mg/kg/day 138 mg/kg/day 277 mg/kg/day 238 mg/kg/day 477 mg/kg/day 0 mg/kg/day	5 days/week for 78 weeks	92-93 weeks	mice/B6C3F1	M M M F F F	18 50 45 45 41 20	liver	Hepatocellular carcinomas were found in 1/18 (6%) control males, 18/50 (36%) low-dose males and 44/45 (98%) high-dose males; in 0/20 control females, 36/45 (80%) low-dose females and 39/41 (95%) high-dose females.	NCI, 1976
Corn oil	0 mg/kg/day 90 mg/kg/day 180 mg/kg/day 100 mg/kg/day[a] 200 mg/kg day[a] 0 mg/kg day	5 days/week for 78 weeks	111 weeks	rats/ Osborne-Mendel	M M M F F F	19 50 50 49 48 20	kidney	Renal carcinomas and adenomas were found in 0/19 control males, 4/50 (8%) low-dose males and 12/50 (24%) high-dose males; 0/20 control females, 0/49 low-dose females and 2/48 (4%) high-dose females. Thyroid tumors were found in 1/20 control females, 8/49 low-dose females and 10/48 high-dose females.	NCI, 1976
Toothpaste[b]	0 mg/kg/day 15 mg/kg day 75 mg/kg/day 165 mg/kg day	6 days/week for 52 weeks	52 weeks	rats/ Sprague-Dawley	M M M M	75 25 25 25	none	No treatment-related neoplastic effects were seen in comparison with controls; however, all groups had a high incidence of pulmonary and renal histopathology.	Palmer et al., 1979
Toothpaste[b]	0 mg/kg/day 15 mg/kg day 75 mg/kg day 165 mg/kg day	6 days/week for 52 weeks	52 weeks	rats/ Sprague-Dawley	F F F F	75 25 25 25	none	Same as above	Palmer et al., 1979

TABLE 4-1 (cont.)

Vehicle	Dose	Duration of Treatment	Duration of Study	Species/Strain	Sex	Number Treated	Target Organ	Effects	Reference
Toothpaste[b]	0 mg/kg/day 60 mg/kg day	6 days/week for 80 weeks	95 weeks	rats/ Sprague-Dawley[c]	M M	50 50	none	No treatment-related neoplastic effects.	Palmer et al., 1979
	0 mg/kg/day 60 mg/kg day				F F	50 50	mammary gland	Mammary tumors were present in 16/20 control females and 21/50 treated mice; however, there were significantly more malignant tumors in the chloroform-exposed mice (p=0.056)[d]	
Toothpaste[b]	0 mg/kg day 17 mg/kg day 60 mg/kg day	6 days/week for 96 weeks	96 weeks	rats/NR	M M M	104 52 52	kidney	Several mice had lymphomas, but the incidence was not related to chloroform exposure. Renal tumors appeared in the high-dose males, but in no other group.	Roe et al., 1979
	0 mg/kg day 17 mg/kg day 60 mg/kg day				F F F	104 52 52	none		

[a]TWA dose reflecting initial dose levels of 250 and 125 mg/kg/day that were lowered to 180 and 90 mg/kg/day after 22 weeks in the high- and low-dose female groups, respectively.

[b]Toothpaste formulation included peppermint oil and eucalyptol (essential oils) as flavor components

[c]Caesarian-delivered, specific-pathogen-free rats

[d]Significance of Fischer exact test as reported by U.S. EPA (1982)

Presumably because chloroform has been a contaminant in toothpaste, British scientists treated rats (Palmer et al., 1979), mice (Roe et al., 1979) and dogs (Heywood et al, 1979) with chloroform in a toothpaste base including essential oils as flavor components. Range-finding studies were performed in all experiments. No effects at dose levels of 15, 17 and 165 mg/kg/day for 52 weeks were reported in rats. When female rats were treated with 60 mg/kg/day for 96 weeks, however, there was an increase ($p=0.056$) in malignant mammary gland tumors in the chloroform-treated group, although the untreated group developed benign mammary tumors (Palmer et al., 1979). There was an increased incidence of kidney tumors in the high dose (60 mg/kg/day) level in male mice (Roe et al., 1979). The females had no increased incidence of cancer, but there appeared to be some confounding influence because of the vehicle. The authors addressed, but did not resolve, the problem of the effect produced by different vehicles (Roe et al., 1979).

4.2.2. Inhalation. Pertinent data regarding the carcinogenicity of inhaled chloroform were not located in the available literature.

4.3. OTHER RELEVANT DATA

Chloroform was not mutagenic in Escherichia coli strains K12, WP2p and WP2uvrA$^-$p or in Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 (Kirkland et al., 1981), with and without metabolic activation (S-9). Chloroform was not mutagenic in cultured Chinese hamster lung fibroblasts at the 8-azaguanine locus (Sturrock, 1977), nor did chloroform increase sister chromatid exchanges in cultured Chinese hamster ovary cells or human lymphocytes (White et al., 1979; Uehleke et al., 1977). In a recent experiment in which chloroform was used at a higher concentration, it was found to induce sister chromatid exchange in cultivated human lymphocytes (Morimoto and Koizumi, 1983). In the presence of metabolic activation

(S-9), chloroform was reported to be weakly positive or "suggestive" in mutagenicity assays in Saccharomyces cerevisiae D7 and Drosophilia, in a host-mediated assay with S. typhimurium, in the murine bone marrow micronucleus test and in the induction of murine sperm head abnormalities (Agustin and Lim-Sylianco, 1978; Callen et al., 1980; Land et al., 1981; Topham, 1980; Gocke et al., 1981).

4.4. WEIGHT OF EVIDENCE

Oral exposure to chloroform has caused hepatic carcinomas in male and female B6C3F1 mice (NCI, 1976), renal carcinomas and adenomas in male Osborne-Mendel rats (NCI, 1976) and in male ICI mice (Roe et al., 1979), thyroid tumors in female Osborne-Mendel rats (NCI, 1976) and an increased incidence of malignant mammary gland tumors after chronic exposure in Sprague-Dawley rats (Palmer et al., 1979). Evidence is sufficient to classify chloroform as an animal carcinogen. Although some association between oral exposure to chloroform (presumably as a result of chlorinating drinking water) and human bladder, intestinal and rectal cancer has been reported (see Section 4.1.1.), the evidence for human carcinogenicity is best designated as limited. Applying the criteria for evaluating the overall weight of evidence of carcinogenicity to humans proposed by the Carcinogen Assessment Group of the U.S. EPA (Federal Register, 1984), chloroform is most appropriately classified as a Group B2, a probable human carcinogen.

5. REGULATORY STANDARDS AND CRITERIA

The ACGIH (1983) recommends a TWA-TLV of 10 ppm (50 mg/m^3) and a STEL of 50 ppm (225 mg/m^3) for chloroform exposure, and also notes that chloroform has induced cancer in animals by the oral route at high and intermediate dose levels and is a suspected carcinogen for humans.

6. RISK ASSESSMENT

6.1. ACCEPTABLE INTAKE SUBCHRONIC (AIS)

Chloroform is known to be carcinogenic to animals and is suspected of being carcinogenic to humans. Data are sufficient for derivation of a q_1^*; therefore, it is inappropriate to derive an AIS for this chemical.

6.2. ACCEPTABLE INTAKE CHRONIC (AIC)

Chloroform is known to be carcinogenic to animals and is suspected of being carcinogenic to humans. Data are sufficient for derivation of a q_1^*; therefore, it is inappropriate to derive an AIC for this chemical.

6.3. CARCINOGENIC POTENCY (q_1^*)

6.3.1. Oral. The Carcinogen Assessment Group (U.S. EPA, 1984) used the following data: liver tumors in female mice (NCI, 1976); liver tumors in male mice (NCI, 1976); kidney tumors in male rats (NCI, 1976); and kidney tumors in male mice (Roe et al., 1979). There was no compelling reason to select any one of these data sets over the others; therefore, the geometric mean of the slopes (q_1^*), 7×10^{-2} $(mg/kg/day)^{-1}$, was selected. The Health Assessment Document on Chloroform (U.S. EPA, 1984) contains a complete discussion of the calculation of the q_1^*.

6.3.2. Inhalation. Pertinent data regarding the derivation of a q_1^* for chloroform inhalation were not located in the available literature.

7. REFERENCES

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